IntegRAted chronic care program at specialized AF clinic versus usual CarE in patients with Atrial Fibrillation, a Multicenter Randomized Controlled Clinical Trial

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Primary Objective: To show that an integrated chronic care program in a specialized AF clinic reduces cardiovascular hospitalizations and mortality.Secondary Objective(s): 1) To demonstrate the benefits of an integrated chronic care program in terms...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON47091

Source
ToetsingOnline

Brief title
RACE 4

Condition

- Cardiac arrhythmias
- Embolism and thrombosis

Synonym
'Atrial Fibrillation' 'Irregular heartbeat'

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Achmea Zorgverzekeraar (Stichting Achmea Gezondheidszorg),Bayer,Boehringer Ingelheim,Bristol-Myers Squibb,DSW Zorgverzekeraar,zorgverzekeraars;farmaceutische industrie

Intervention

Keyword: Atrial Fibrillation, Atrial Fibrillation guideline, Chronic care program, Nurse specialist

Outcome measures

Primary outcome

The primary endpoint is a composite, defined as unplanned admission to the

hospital for any cardiovascular reason and cardiovascular death.

The endpoint events leading to unplanned hospitalisation or death are

therefore:

1. Left or right ventricular heart failure which is independent of LVEF

(preferably confirmed by biomarker assessment using NT-pro-BNP) and requiring

intravenous diuretics or an unplanned hospitalisation without admission when

any adjustment of heart failure therapy suffices;

2. Ischemic thromboembolic complications including stroke (the sudden onset of

a focal neurologic deficit in a location consistent with the territory of a

major cerebral artery caused by an arterial thrombus in this artery,

categorized as ischemic stroke and TIA (transient stroke, whereby clinical

symptoms disappear within 24 hours))confirmed by a neurologist on the basis of

computerised tomography or MRI; peripheral emboli, pulmonary emboli or systemic

emboli (an acute vascular occlusion of an extremity or organ) documented by means of imaging, surgery or autopsy;

3. Acute coronary syndrome (STEMI/ NSTEMI/ unstable angina pectoris, with at least two of the following characteristics: (1) typical chest pain for at least 20 minutes; (2) ischemic electrocardiographic changes, and (3) cardiac enzyme elevation more than twice the upper limit of normal or instable angina pectoris, respectively documented on ECG as well as/ or only in blood levels of key chemical markers);

4. Major bleeding(an acute bleeding with the hemoglobin value decreased by > 20 g/ L (>2g/ dL; 1,2 mmol/l), or requiring blood transfusion of at least two units of blood, or a symptomatic bleeding in a critical organ or area (intra-cranial (intracerebral hemorrhage, subdural hemorrhage or subarachnoid hemorrhage), retroperitoneal, spinal, ocular, pericardial, or a traumatic articular) or fatal bleeding;

5. Arrhythmic or potential arrhythmic events (atrial fibrillation, -flutter, other supraventricular rhythm or sustained ventricular tachycardia confirmed by ECG, > 30 sec), syncope (a sudden temporary loss of consciousness associated with a loss of postural tone with spontaneous recovery not requiring electrical or chemical cardioversion) or cardiac arrest (circulatory arrest necessitating resuscitation and hospitalisation) or an unplanned hospitalisation without admission with any adjustment required to rate or rhythm control therapy, and

6. Life-threatening adverse effects of rate or rhythm controlling drugs (any pro-arrhythmia of Vaughan Williams classes I and III anti-arrhythmic drugs, digitalis intoxication, drug-induced heart failure or conduction disturbances required hospitalisation);

Cardiovascular deaths were classified according to a modified Hinkle and Thaler classification (Hinkle et al., 1982).

Cardiovascular mortality

Death from a diagnosed cardiovascular cause, classified as cardiac arrhythmic, cardiac non-arrhythmic, or a vascular non-cardiac cause.

Cardiac, arrhythmic

Death from rapid ventricular tachycardia or fibrillation and had this rhythm not occurred the patient would have probably survived for at least 4 months. Loss of cardiac output and pulse is sudden and precedes collapse of the circulation (defined as a state of very low cardiac output, poor peripheral perfusion, systolic blood pressure of less than 80 mm Hg, or dependence on intravenous inotropic support) or severe pulmonary oedema, characterised by severe respiratory distress of sudden onset without evidence of non-cardiac cause. The patient is not already in shock or pulmonary oedema at the time of onset of the arrhythmia.

Cardiac, non-arrhythmic

The patient develops collapse of the circulation or is in shock or severe pulmonary oedema before loss of cardiac output and fatal arrhythmia. Special categories included monitored patients who had profound bradycardia or asystole, or a rhythm generally compatible with normal cardiac output, and, therefore, probably electromechanical dissociation, immediately before abrupt circulatory collapse.

Vascular, non-cardiac

For example, aortic dissection, ruptured aneurysm, other haemorrhage, cerebral vascular accident, pulmonary embolus.

Definitions for the components of the primary endpoint

Cardiovascular mortality

Death from a diagnosed cardiovascular cause, classified as cardiac arrhythmic, cardiac non-arrhythmic, or a vascular non-cardiac cause.

Heart failure

Heart failure independent of LVEF (preferably confirmed by biomarker assessment using NT-pro-BNP) necessitating hospitalisation and requiring intravenous diuretics, or other adjustments of heart failure therapy during hospitalisation.

Stroke

A disabling hemorrhagic, ischemic, or undetermined stroke confirmed by a neurologist on the basis of computerised tomography or magnetic resonance imaging and necessitating hospitalisation.

Systemic emboli

An acute arterial occlusion of an extremity or organ. Have to be confirmed by a physician, typically with some type of imaging and necessitating hospitalization.

Acute coronary syndrome

STEMI/ NSTEMI Myocardial infarction with at least 2 of the following: (1) typical chest pain for at least 20 minutes; (2) electrocardiogram showing changes of acute myocardial infarction; and (3) cardiac enzyme elevation more than twice the upper limit of normal or instable angina pectoris, respectively documented on ECG as well as/or only in blood levels of key chemical markers, necessitating hospitalisation.

Bleeding

A bleeding with the hemoglobin value decreased by > 20 g/ L (>2g/ dL) or requiring blood transfusion or symptomatic bleeding in a critical organ or area (intra-cranial, retroperitoneal, spinal, ocular, pericardial, or a traumatic articular) or fatal.

Arrhythmic events

Includes episodes of atrial fibrillation and syncope, necessitating hospitalisation, or adjustments in rate- or rhythm control therapy during hospitalisation.

Syncope

A sudden temporary loss of consciousness associated with a loss of postural tone with spontaneous recovery not requiring electrical or chemical cardioversion.

Sustained ventricular tachycardia

Lasting more than 30 seconds and must be documented on electrocardiogram (ECG) and requires hospitalization.

Cardiac arrest

Circulatory arrest necessitating resuscitation and hospitalization.

Life-threatening adverse effects of rate or rhythm controlling drugs

Pro-arrhythmia of classes I and III anti-arrhythmic drugs, digitalis intoxication, drug-induced heart failure or conduction disturbances and ventricular arrhythmias necessitating hospitalisation.

Secondary outcome

The secondary endpoints are:

1. The cost benefit of the intervention by means of a cost effectiveness analysis;

2. The extent to which the comprehensive cardiovascular treatment is in

accordance to the latest ESC guidelines for AF, HF guidelines

of acute and chronic heart failure and CVD Prevention guidelines;

3. Patient quality of life and satisfaction;

4. Patient anxiety and/ or depression;

5. Patients* knowledge of AF and

6. Patients* compliance in medication.

Study description

Background summary

The treatment of patients with atrial fibrillation is often inadequate due to bad adherence to the guidelines.
Especially the poor guideline adherence in relation to the use of antithrombotic therapy is leading to increased morbidity and mortality in patients with atrial fibrillation.

In order to improve outcomes for patients with AF, an integrated chronic care program (ICCP) for patients with AF was developed in the Maastricht University Medical Center. The program consists of a nurse-driven, guideline-based, software-supported ICCP for patients with atrial fibrillation in the outpatient specialized AF Clinic. Effects of the program were compared with routine cardiac care for patients with newly diagnosed AF in a large outcomes study with 712 patients.

The combined endpoint of cardiovascular hospitalization and cardiovascular death showed a relative risk reduction of 35% by nurse-led care (14,3% nurse led care compared to 20,8% usual care, hazard ratio 0,65; 95% CI, 0,45 to 0,93; $p<0,05$). The adherence to guideline recommendations was significantly better in the nurse-led care group. This ICCP for patients with AF represents the combined beneficial effect of the disease management system in a single centre trial.

In addition to these outcomes a multicenter trial is needed to study if the results are generalizable to other hospitals where an Integrated Chronic Care Program at a specialized AF clinic is implemented.

It is hypothesized that treatment at a specialized AF clinic is superior to usual care in terms of cardiovascular mortality, cardiovascular hospitalizations and cost effectiveness.

Study objective

Primary Objective:
To show that an integrated chronic care program in a specialized AF clinic reduces cardiovascular hospitalizations and mortality.

Secondary Objective(s):
1) To demonstrate the benefits of an integrated chronic care program in terms of cost effectiveness expressed in quality adjusted life years (Qualy*s). 2) To demonstrate process outcomes in terms of guideline adherence and comprehensiveness of cardiovascular treatment: the extent to which treatment is delivered according to the latest ESC AF guidelines and modified for the Netherlands, the HF guidelines of acute and chronic heart failure and the CVD Prevention guidelines; 3) To demonstrate that an integrated chronic care program in a specialized AF clinic improves quality of life (including anxiety and depression) and patient satisfaction; 4) To demonstrate that patient knowledge improves significantly better in the intervention group and by that reduces hospitalizations and cardiovascular mortality; 5) To show that patient compliance in medication improves significantly using personal electronic guidance through Medical manager* (developed by R. Pisters, MUMC) in the intervention group.

Study design

The RACE4 is an event driven study. A total number of 246 events is needed. The study is divided in two arms: a control arm (usual care provided by the cardiologist) and an intervention arm (integrated chronic care program at a specialized AF clinic) in 8 hospitals in the Netherlands. In total 1716 patients with newly diagnosed AF will be included. The total duration of the study is 6,5 years. The inclusion of patients will start at the 1st of December 2012. The foreseen recruitment period concedes till june 2018 and follow-up till June 2019. Data will be collected at inclusion, after 3 months, 6 months, 12 months and every year thereafter. Patients in the intervention group will be seen at 3 months after the first appointment at the AFclinic, will get a phonecall at 6 months and thereafter annually monitoring at the AF clinic. Control at the cardiologist will be planned advised by the cardiologist.

Intervention

The intervention in this study contains the treatment through an integrated chronic care program at the specialized AF clinic. The ICCP consists of a nurse specialist, cardiologist, guidelines-based software supported program,

web-based patient centered management of patient*s own medication and tailored telemonitoring at an outpatient AF clinic.

Study burden and risks

Patients in the control group and intervention group will not have any risk or burden for participation in the study. Patients in the control group will receive care as usual and patients in the intervention group will receive care through an integrated chronic care program for AF. Data of the pilot study at the University Hospital of Maastricht with 712 patients, presented at the ACC 2011, showed a relative risk reduction of 35% in the combined endpoint of cardiovascular hospitalization and cardiovascular death with patients at the specialized AF clinic compared to the usual care at the cardiologist. The adherence to the AF guideline recommendations was significantly better at the AF clinic.
The study group is not aware of any potential risk or burden for the patient in the intervention group (specialized AF clinic). The pilot suggests that the ICCP at the specialized AF clinic will improve patient treatment and a risk reduction in cardiovascular hospitalization and death.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patients with newly diagnosed AF detected on electrocardiogram (ECG), holter recordings or eventrecorder with a duration > 30 seconds, 3 months before inclusion;
2. Patients with a history of diagnosed AF, with no regular control at a cardiologist for AF in the last
2 years and referred by a non-cardiologic medical specialist for new diagnostics or therapeutic issue;
3. Age * 18 years.

Exclusion criteria

1. No electrocardiographic objectified AF;
2. Unstable heart failure defined as NYHA IV or heart failure necessitating hospital admission < 3 months before inclusion;
3. Acute coronary syndrome (acute myocardial infarction or instable angina pectoris, with two of the following characteristics: chest pain and/ or ischemic electrocardiographic changes, and/ or cardiac enzyme rise) < 3 months before inclusion;
4. Untreated hyperthyroidism or < 3 months euthyroidism before inclusion;
5. Foreseen pacemaker, internal cardioverter defibrillator (ICD), and/ or cardiac resynchronization therapy (CRT);
6. Cardiac surgery * 3 months before inclusion;
7. Planned cardiac surgery;
8. Regular control and treatment, also for AF, at another specialized outpatient cardiac clinic;
9. Patient is not able to fill in the questionnaires;
10. Participation in other clinical study.

Study design

Design

Study type:	Interventional
Intervention model:	Other

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-12-2012
Enrollment:	1716
Type:	Actual

Ethics review

Approved WMO Date:	04-04-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-09-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-10-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-10-2012

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-09-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-10-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-11-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-04-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	02-01-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01740037
CCMO	NL39000.068.11

Study results

Date completed: 01-10-2018

Results posted: 19-11-2019

Actual enrolment: 1375

First publication
23-09-2019